Circulatory Effects of Dobutamine and Dopamine in Dogs Following Experimental Injury of the Sino-Atrial Node

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Circulatory Effects of Dobutamine and Dopamine in Dogs Following Experimental Injury of the Sino-Atrial Node

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Introduction

The sympathomimetic amines are still one of the primary forms of therapy in the low cardiac output syndrome[5)13)19)], severe heart failure[1)3)], and other conditions[19)25)]. The hemodynamic actions of dopamine, two synthetic catecholamines have been, extensively investigated in recent years[7)10)12)21)22)26)]. Dopamine, the third endogenous catecholamine and the immediate precursor of norepinephrine, also has unusual cardiovascular actions that appear to be due to its effect on a specific vascular receptor[4)6)16)]. It increases myocardial contractility and heart rate by direct action on β-adrenergic receptors, but it still produces ventricular arrhythmia[16)]. Dobutamine is a new synthetic sympathomimetic amine developed in an effort to obviate the deleterious effects associated with current available inotropic agents[24)] Recent studies indicate that it dramatically improves cardiac output with relatively little chronotropic or peripheral vascular effect[11)18)]. However, it differs from dopamine that it does not selectively dilate the renal vascular beds[11)22)]. There is no report, as far as we know, on the hemodynamic effects of these two agents in states of S-A node dysfunction. Experimental injury of the S-A node resulted in a low cardiac outpput state. Dobutamine and dopamine were then injected intravenously in various concentrations. The purpose of the present study is to compare in a group of dogs with experimental S-A node injury the degree of functional cardiovascular response to these two agents[2)].

Meterials and Methods

Ten mongrel dogs weighing 7.5-14.5 kg. were anesthetized with intravenous Nembutal (25-30mg/kg). Each dog was ventilated with room air via an endotracheal tube attached to a Harvard pump respirator. A control electrocardiogram was recorded continuously.

Key words Sino-atrial (S-A) node injury, Dobutamine, Dopamine, Lidocaine.
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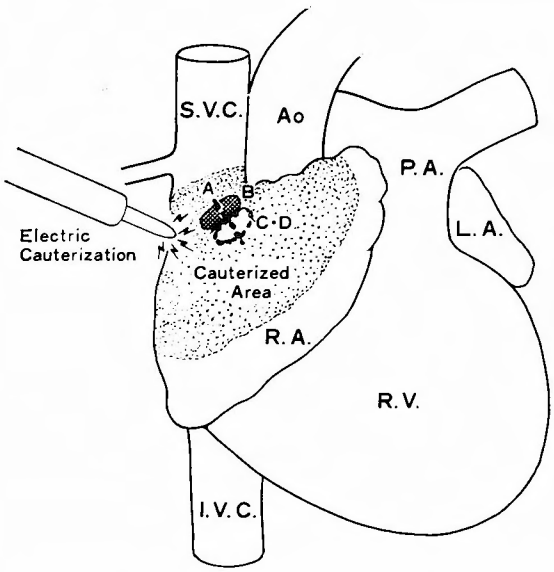


Location of S-A node : dotted line A was proposed by Keith & Flack in 1907, closed circle B by Lewis in 1925, opened circle C & D by Koch & Bachman in 1911 and 1923, respectively.

Electrocauterization was performed over the dotted area shown in the figure.

S. V. C.=Superior Vena Cava
I. V. C.=Inferior Vena Cava
Ao=Aorta
P. A.=Pulmonary Artery
R. A.=Right Atrium
R. V.=Right Ventricle

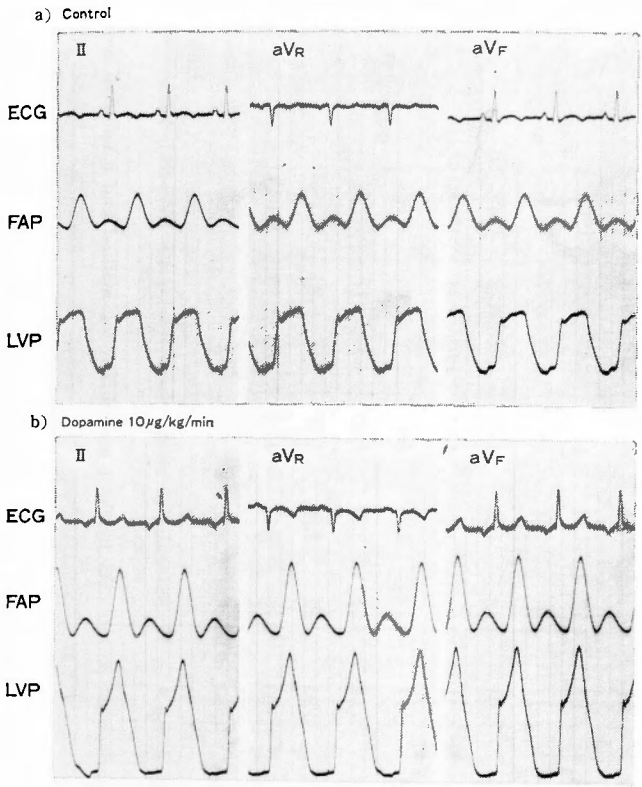
Fig. 1. Experimental injury of S-A nobe by electrocauterization

The chest was then opened via a right thoracotomy through the 3rd or 4th intercostal space. The lung was retracted backwards. The pericardial sac was opened in front of the phrenic nerve and retracted with stay sutures. Femoral arterial pressure was recorded through a fluid-filled catheter which had been tuned and optimised to promote linear frequency responses up to 16 Hz. Left ventricular pressure was measured with Statham's physiological pressure transducer (model no. SF 1) which was directly inserted into the left ventricle through an incision wound at the apex. These frequency responses have been shown to provide data necessary to obtain high quality dp/dt measurements. All of the transducers were conected to a SAN-EI Polygraph PH 41-6 which gives a continuous display and can be pushed to record when necessary. Central venous pressure was set up through the right external jugular vein. Cardiac output was measured by Statham's electromagnetic flowmeter (model SP-201) with its probe placed around the ascending aorta. A Neo-med solid state electrosurgery model 3000 (15 VAC 50/10 Hz 15A) was used. Electrocauterization was performed with a coagulation power of 20 joules around the junction of the superior vena cava and the right atrium which produced a visible area of cauterization about 0.5 to 1.0 cm in diameter (Fig. 1). After an inverted P wave, a junctional rhythm and / or a slower sinus rate was recognized in the ECG, all measurements were recorded (Fig. 2).

Dobutamine and dopamine (5, 10, 15, 20, 30, 40, and 50 μg/kg/min) were given, each dose level for 15 minutes, starting with either drug in random order with equilibrium intervals of at least 15 minutes between the different drug infusions.

Results

The cardiac output change is shown in Fig. 3. The percentage change was calculated and drawn on a plotgram. Nearly all of the lines rise and fall in a linear way.



a) Before S-A node injury.
b) During dopamine infusion after S-A node injury.
ECG shows inverted P wave and slower heart rate.
ECG : Electrocardiogram
FAP : Femoral Arterial Pressure
LVP: Left Ventricular Pressure

Fig. 2. Measurements before and after S-A node injury with an example of dopamine infusion

The heart rate was more stable with dobutamine than with dopamine (Fig. 4), though neither of them caused severe tachycardia. Sinus tachycardia was observed in the group without S-A node injury. However, tachycardia of ventricular origin (sometimes multifocal) were observed in the group with S-A node injury.

The systolic pressure changed in a rather steady and linear way in the dogs infused with dobutamine in both the controls (the same dogs before injury of the S-A node but after opening of the chest and pericardium) and the S-A node injuried group. (Fig. 5).

All values were examined statistically (Table 1-6). Most of these results are statistically significant. All t-test compared effects of dopamine and dobutamine in the same group. The statistical analyses were performed using paired data t test by difference method, and a p value of less than 0.05 was taken as indicative of statistical significance[2].

As mentioned above, drug induced cardiac arrhythmias especially of ventricuar origin were recognized in the group with S-A node injury, but dopamine seemed to cause them more earily, either with respect to drug dosage or frequency and or severity of arrhythmia. The dosage effect was about twofold; i. e. dopamine 15 μg/kg/min was equivalent to dobutamine 30 μg/kg/min. Normal rhythm was restored after discontinuing the intravenous infusion for several minutes (Fig. 6). However, in cases of severe arrhythmia, administration of lidocaine 3 mg/kg in bolus injection was necessary within 30 to 60 seconds after the bolus injection, a decrease in the ventricular irritability was usually observed. Sometimes lidocaine was used continuously in the intravenous drip to control the arrhythmia caused by these two agents. Lidocaine was very effective against ventricular arrhythmias especially multifocal ventricular extrasystoles and ventricular tachycardia.

Table 1　Change of cardiac index (before S-A node injury)

												Mean ± SE	%	p value
B. W. (Kg.)		13.4	8.3	7.5	12.3	14.5	9.7	10.5	9.0	8.5	12.0	10.6		
BSA (m^2)		0.632	0.459	0.429	0.597	0.666	0.509	0.537	0.485	0.466	0.587	0.540		
Control		2.06	2.18	2.10	2.76	2.70	2.36	2.42	2.27	1.76	2.56	2.33±0.05	100%	
5γg kg min.	Dp	2.75	3.53	2.31	3.50	4.13	3.56	3.97	3.15	2.23	3.49	3.28±0.17	141%	p>0.20*
	Dt	3.16	2.75	2.73	3.41	3.46	4.08	3.91	2.78	2.64	4.26	3.34±0.14	143%	
10γg kg min.	Dp	3.13	4.01	2.84	4.37	3.92	4.38	4.25	3.13	3.03	4.32	3.75±0.17	161%	p>0.20*
	Db	3.82	3.01	2.94	3.96	3.75	4.19	4.97	3.18	2.64	4.77	3.76±0.18	162%	
15γg/kg min.	Dp	3.78	4,58	3.25	5.39	4.43	4.68	5.51	4.12	3.54	4.91	4.43±0.21	190%	0.10>p>0.05*
	Db	3.97	3.99	3.48	4.77	4.13	4.52	5.12	4.08	3.11	4.86	4.22±0.47	181%	
20γg/kg min.	Dp	3.70	4.25	3.03	5.61	4.50	4.32	5.59	4.43	3.26	4.26	4.32±0.22	185%	p<0.05**
	Db	3.89	4.68	3.85	5.78	4.73	4.68	5.31	4.95	3.35	4.91	4.62±0.21	198%	
30γg/kg min.	Dp	3.24	3.77	2.91	5.24	3.98	3.63	5.72	4.12	2.75	4.01	3.96±0.26	170%	p<0.02**
	Db	3.80	4.03	3.73	5.36	4.50	4.62	5.21	4.33	3.39	4.60	4.37±0.17	188%	
40γg/kg min.	Dp	2.93	3.59	2.80	4.29	3.30	3.24	4.93	3.81	2.75	4.17	3.58±0.23	154%	p<0.01**
	Db	3.60	3.70	3.50	4.51	4.13	4.13	5.03	3.67	3.07	4.34	3.98±0.15	171%	

Dp : dopamine　Db : dobutamine　SE : Standard Error of the mean

BSA (Body surface area) of dog = $0.112 \times \sqrt[3]{(BW\ kg)^2}$

(from "The estimation formulae of the body surface area of the Japanese dog." by N. Shiraishi, et al. in Nissin Igaku 43 : 361-365, 1956.)

* : $p>0.05$, not significant　** : $p<0.05$, significant

t test between dopamine and dobutamine in the same group (comparison of paired data by the t test, difference method and a value of less than 0.05 was taken as indicative of statistical sigificance)

Table 2 : Changes of Cardiac index (after S-A nobe injury)

											Mean±SE	percentage	p value
B. W. (kg.)		7.8	9.0	8.5	12.4	11.0	13.0	10.5	7.5	12.0	11.3	10.3		
BSA (m^2)		0.441	0.485	0.466	0.666	0.554	0.619	0.537	0.429	0.587	0.564	0.530		
Control		1.90	2.27	2.04	2.55	2.53	2.67	2.33	2.33	2.98	2.75	2.46±0.01	100%	
After nodal injury		1.45	1.44	1.46	2.08	1.99	2.02	1.62	1.75	1.79	1.83	1.73±0.11	72%	p<0.001**
5γg/kg min	Dp	2.31	1.75	1.52	2.12	2.08	2.58	2.23	2.33	2.64	1.93	2.16±0.08	88%	p>0.20 NS*
	Db	2.34	1.61	1.72	2.08	1.99	2.13	1.79	2.21	2.62	2.39	2.09±0.10	85%	
10γg/kg/min	Dp	2.38	1.86	1.61	2.33	2.17	2.99	2.98	3.03	3.19	2.54	2.52±0.15	103%	p>0.20 NS*
	Db	2.43	2.33	1.76	1.95	2.56	2.54	2.50	3.01	3.12	2.78	2.49±0.15	102%	
15γg/kg/min	Dp	2.20	2.06	1.72	2.83	2.53	3.07	3.72	3.26	3.42	2.68	2.73±0.23	111%	p>0.20 NS*
	Db	2.31	2.87	2.02	2.37	2.96	2.73	2.92	2.98	3.32	2.84	2.74±0.10	111%	
20γg/kg/min.	Dp	2.15	2.47	2.06	2.57	2.44	2.50	3.07	2.56	2.84	2.78	2.55±0.08	104%	p<0.01**
	Db	2.47	3.63	2.83	1.90	3.83	2.83	3.31	3.82	3.70	3.55	3.16±0.25	129%	
30γg/kg/min.	Dp	1.81	2.35	2.08	2.55	2.35	2.42	2.79	2.33	2.64	2.39	2.38±0.05	97%	p<0.001**
	Db	2.74	3.61	3.22	1.75	4.60	3.31	3.63	4.50	4.57	3.72	3.54±0.32	144%	
40γg/kg/min.	Dp	1.81	1.55	2.06	2.33	1.62	2.10	1.90	1.75	1.91	2.04	1.92±0.01	78%	p<0.001**
	Db	3.06	3.40	2.90	1.58	4.03	3.23	3.48	4.01	4.26	3.55	3.32±0.28	135%	

Dp : dopamine Db dobutamine

* : NS=Not significant ** : Significant

Table 3 : Changes in heart rate (before S-A node injury)

											Mean±SE	%	p value
B. W. (kg.)		13.4	8.2	7.5	12.3	14.5	9.7	10.5	9.0	8.5	12.0	10.6		
Control		79	134	125	111	98	148	116	132	121	83	114± 7	100%	
5 μg kg min	Dp	87	192	169	118	133	187	144	171	163	96	146±12	127%	p<0.001
	Db	80	166	155	113	108	153	124	143	152	93	129± 9	112%	
10 μg kg min	Dp	97	184	186	135	147	210	161	184	176	114	159±11	139%	p<0.001
	Db	82	164	160	115	108	150	124	140	150	90	128± 9	112%	
15 μg/kg/min	Dp	102	216	192	142	156	215	163	190	178	114	167±12	145%	p<0.001
	Db	86	170	162	120	108	156	126	144	150	88	131±10	114%	
20 μg kg min	Dp	102	224	198	156	158	220	172	198	188	120	174± 7	151%	p<0.001
	Dp	86	174	160	130	108	158	128	162	156	100	136±10	119%	
30 μg/kg/min	Dp	110	224	200	158	154	210	170	196	182	118	172±12	150%	p<0.001
	Db	88	176	170	148	112	164	130	168	158	102	142±10	124%	
40 μg kg min	Dp	110	220	202	162	160	220	182	214	194	124	179±11	156%	p<0.001
	Db	86	180	172	168	114	162	142	178	176	108	149±11	130%	

Dp dopamine Db dobutamine t-test all significant

Table 4 : Changes in heart rate (after S-A node injury)

											Mean±SE	%	p value
B. W (kg.)		7.8	9.0	8.5	12.4	11.0	13.0	10.5	7.5	12.0	11.3	10.3		
Control		100	143	142	88	103	81	120	139	106	94	112± 8	100%	
After nodal injury		88	125	126	73	80	71	88	113	84	80	93± 7	83.2%	p<0.02
5 μg kg min	Dp	94	160	150	84	106	92	98	138	108	90	112± 9	100%	p<0.02
	Db	88	129	121	80	88	73	107	119	84	86	98± 6	87%	
10 μg kg min	Dp	124	178	158	102	126	106	112	148	148	114	132± 8	118%	p<0.001
	Db	92	130	128	81	90	75	110	121	87	90	100± 6	90%	
15 μg kg min	Dp	130	200	164	113	156	110	128	178	148	122	145± 9	130%	p<0.001
	Db	84	145	126	82	91	76	112	124	88	92	102± 7	91%	
20 μg kg min	Dp	142	200	180	115	170	112	136	180	148	128	152± 9	135%	p<0.001
	Db	78	148	128	84	96	82	118	130	92	96	105± 8	94%	
30 μg kg min	Dp	150	216	196	124	188	116	154	182	154	132	161±11	144%	p<0.001
	Db	76	166	138	94	100	92	134	138	90	108	114± 9	102%	
40 μg kg min	Dp	160	238	210	128	174	124	182	206	160	138	172±12	154%	p<0.001
	Db	70	186	152	98	112	102	138	142	102	114	122±11	109%	

Dp dopamine Db : dobutamine t-test . all significant

Table 5 : Changes in blood pressure (before S-A node injury)

											Mean ± SE	Percentage	p value
B. W. (kg.)		13.4	8.3	7.5	12.3	14.5	9.7	10.5	9.0	8.5	12.0	10.6		
Control		155/92	120/80	180/150	175/140	160/100	120/50	135/68	150/80	196/104	100/40	149±10	100%	
5 μg/kg/min	Dp	205/120	148/83	200/150	170/113	166/105	104/40	120/45	130/60	250/120	110/60	161±14	108%	0.02<p<0.05
	Db	180/150	150/75	195/140	170/95	155/80	106/40	115/60	122/61	238/110	105/45	154±13	103%	
10 μg/kg/min	Dp	244/160	174/90	240/170	180/150	155/80	107/40	142/89	152/94	290/120	160/80	188±13	126%	p<0.02
	Db	192/148	160/75	205/148	182/90	164/84	104/59	132/60	134/73	258/100	105/50	164±15	110%	
15 μg/kg/min	Dp	254/170	180/110	250/180	198/170	200/145	128/52	156/110	173/120	317/150	180/110	198±24	133%	p<0.02
	Db	220/160	164/80	228/160	186/80	188/88	116/55	140/63	146/84	265/132	128/60	178±15	120%	
20 μg/kg/min	Dp	264/175	193/140	260/180	206/175	221/158	144/90	197/148	228/115	330/165	140/60	218±18	147%	p<0.001
	Db	228/165	160/82	218/160	197/90	180/86	124/68	144/52	140/60	265/130	130/70	179±14	120%	
30 μg/kg/min	Dp	260/180	224/160	280/190	280/200	274/170	156/95	220/160	220/135	324/185	170/80	241±16	162%	p<0.001
	Db	220/160	150/80	215/150	190/90	180/90	128/70	148/52	140/80	260/130	120/70	175±15	117%	
40 μg/kg/min	Dp	262/180	200/140	240/180	260/200	260/180	140/90	225/170	210/130	300/200	160/80	226±15	151%	p<0.001
	Db	200/160	152/80	210/140	190/90	180/80	112/70	140/50	130/80	240/130	118/75	167±14	112%	

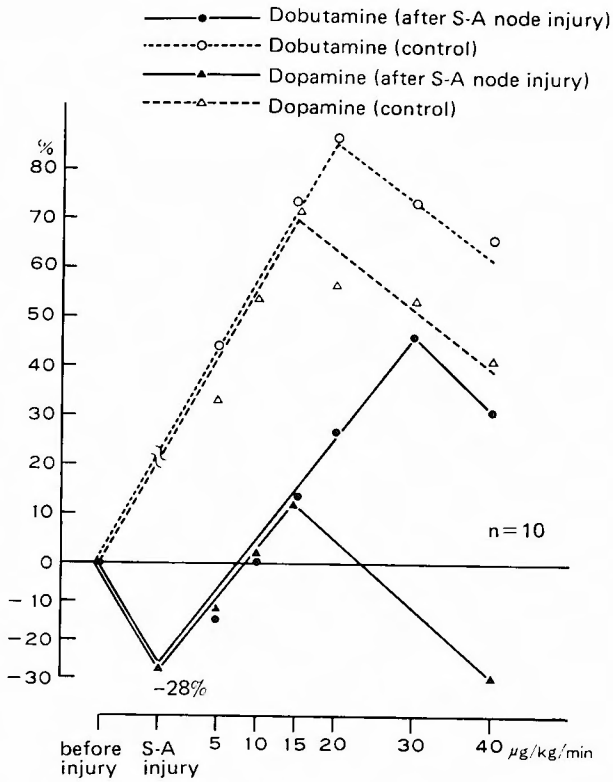
* t-test : all significant

Dp : dopamine Db : dobutamin

Table 6 . Changes in blood pressure (after S-A node injury)

										Mean± SE	%	p value
B. W. (kg.)	7.8	9.0	8.5	12.4	11.0	13.0	10.5	7.5	12.0	11.3	10.3		
Before nodal injury	142/80	180/80	130/66	163/92	180/130	160/65	125/60	130/77	155/95	140/80	151± 5	100%	
After injury	129/75	144/80	104/65	122/80	170/110	150/80	100/40	128/70	125/85	130/65	130± 7	86.5%	p<0.01**
5 μg kg min	Dp 148/68	190/80	142/48	160/80	180/130	155/85	125/60	148/100	135/80	148/80	153± 7	102%	0.02<<p<0.05**
	Db 143/70	170/75	127/70	147/65	168/90	166/90	120/62	140/73	135/65	140/85	146± 4	97%	
10 μg(kg/min	Dp 150/58	198/80	155/85	160/90	190/130	170/90	130/80	157/110	143/87	145/95	160± 6	106%	0.20<p<0.10 *NS
	Db 150/54	168/72	130/80	150/75	190/122	192/104	125/60	145/70	146/75	155/85	155± 7	103%	
15 μg/kg/min	Dp 160/78	198/80	180/64	180/102	190/120	175/90	135/85	195/120	152/90	150/100	172± 5	114%	0.02<p<0.05**
	Db 155/58	176/85	138/60	155/68	195/108	194/108	130/68	160/85	150/80	160/90	161± 8	107%	
20 μg/kg/min	Dp 180/98	200/90	182/85	204/100	210/150	178/100	140/80	185/140	186/130	165/120	183± 6	122%	0.02<p<0.05**
	Db 160/78	194/83	146/70	180/85	220/165	190/105	145/72	165/94	160/90	162/90	172± 8	114%	
30 μg/kg/min	Dp 220/110	236/105	202/90	220/105	220/120	180/110	170/80	192/150	200/148	170/120	201± 7	134%	p<0.01**
	Db 168/90	196/80	153/75	194/105	240/170	180/100	145/75	160/75	153/85	160/95	175± 9	116%	
40 μg/kg/min	Dp 215/120	256/125	238/95	240/110	250/160	215/100	195/100	230/175	254/140	175/100	227± 8	151%	p<0.001*
	Db 166/84	203/104	143/55	192/98	248/153	175/100	142/68	140/72	170/100	150/90	173±11	115%	

Dp : dopamine　Db : dobutamine　*p>0.10　NS : Not significant　**Others : all significant



Control=before injury of the S-A node

After injury of the S-A node, cardiac output decreased by about 30% of the pre-injury control value. Dobutamine infusion 30 μg/kg/min raised cardiac output about +50% above the control value, while dopamine 15 μg/kg/min increaed it only +15%. These post-injury data were different from the control values obtained before S-A node injury.

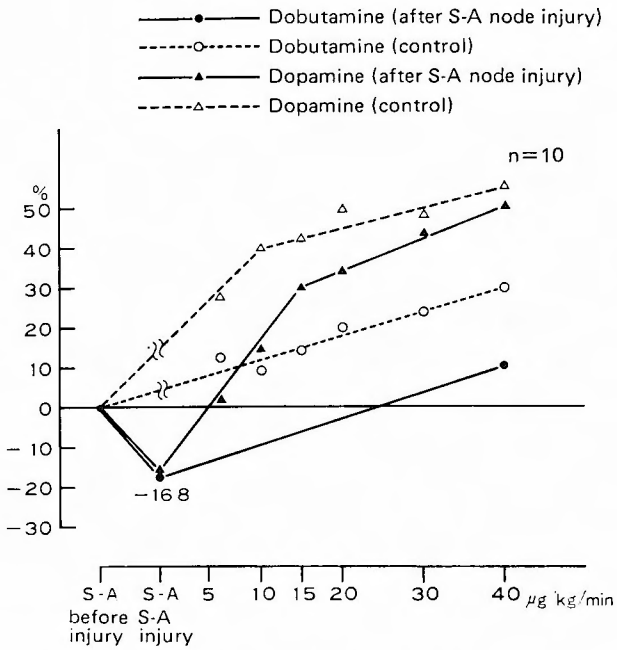
Fig. 3. Cardiac output change with & without S-A node injury during dobutamine and dopamine infusion

The left ventricular pressure gradually increased after lidocaine injection in dobutamine but not dopamine induced arrhythmia. (Fig. 7 a), b))

No hypotension occurred during our experiments. There were no significant hemodynamic differences related to the random order of drug administration.

Discussion

Catecholamines are among the most popular drugs used in the treatment of cardiogenic low output states. The ideal drug in the treatment of low output state would be one which increases cardiac output significantly without causing peripheral vascular constriction or cardiac arrhythmia or tachycardia. Some catecholamines which induced arrhythmia and/or tachycardia have been difficult to use clinically, and some have even been abandoned.



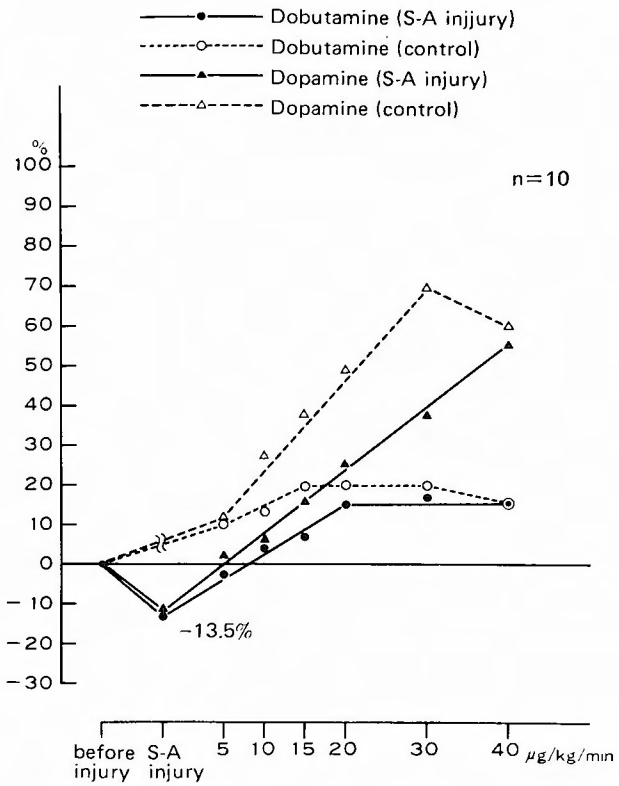
The heart rate decreased 16.8% after S-A node injury. After catecholamine infusion, the heart rate increased gradually with increasing dosage. Dopamine had a stronger chronotropic action than dobutamine. However, neither caused severe tachycardia. The tachycardias were of sinus origin in the control group, but were ventricular or multifocal in the experimental group with S-A node injury.

Fig. 4. Change in heart rate

We are interested in the new synthetic catecholamine, dobutamine, which improves cardiac output with relatively little chronotropic and peripheral vascular effect. So relatively large doses of dobutamine were given with experimental S-A node injury. Cardiac output, blood pressure and heart rate were compared with the values obtained in dogs infused with dopamine.

Experimental S-A node injury caused a low output state, which dobutamine effectively and impressively controlled. With little chronotropic effect, only mild cardiac arrhythmia and tachycardia, and a slightly elevated blood pressure, the cardiac output increased satisfactorily. In these aspects, dobutamine was shown to be superior to dopamine in dogs with S-A node injury.

In the present study, dopamine seemed to induced arrhythmia more easily than did dobutamine, with about half the dose. In most cases arrhythmia could be controlled by lidocaine injection. Moreover, lidocaine in the treatment of dopamine-induced arrhythmia caused a relatively lower left ventricular pressure than when it was used in conjunction with dobutamine.

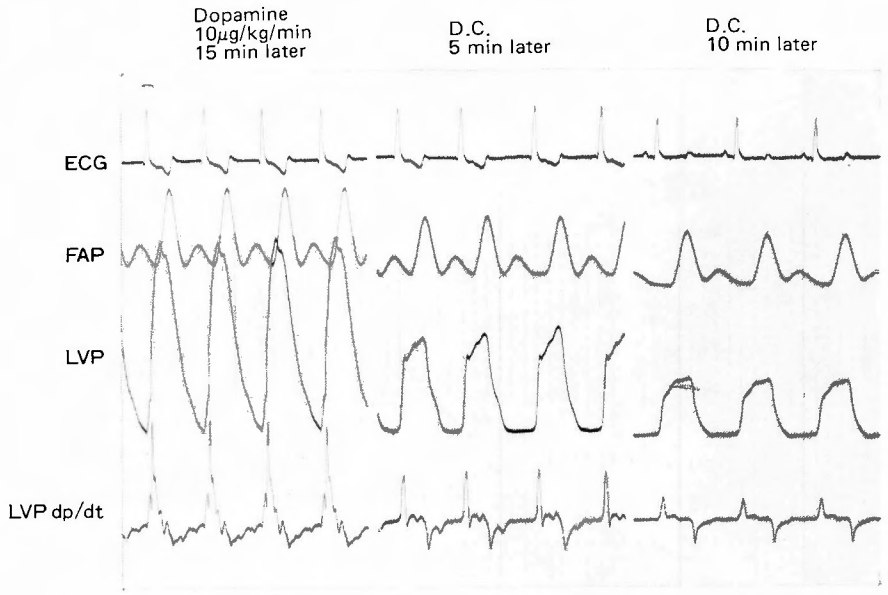


The systolic pressure dropped about 13.5% after S-A node injury. It increased after infusion of different doses of dopamine and dobutamine. Dopamine raised systolic pressure more than did dobutamine both before and after S-A node injury.

Fig. 5. Change in systolic pressure

In this study, dobutamine was superior to dopamine in dogs with S-A node injury. Although there appeares to be little benefit in myocardial economy from dobutamine when compared with isoprenaline in patients following cardiac surgery[17], unlike dopamine or isoprenaline, dobutamine does not rely for part of its action on release of stored catecholamine which may be severely depleted during chronic heart failure or after cardiopulmonary bypass.

Animal studies have demonstrated that dobutamine causes less increase in infarct size than other inotropic agents, probably because of a combination of slower heart rate, coronary vasodilatation and maintenance of aortic diastolic perfusion pressure[20]. Since both heart rate and arterial pressure are major determinants of myocardial oxygen consumption[8][23], dobutamine should be a potentially useful drug in the treatment of low output states, especially in coronary heart disease or sick sinus syndrome. Dobutamine may be of some special value in patients with sick sinus syndrome when hypotension and/or renal function are not serious problems. Otherwise, dopamine may be used effectively.



Left panel Ventricular tachycardia (190 beats/min) was observed 15 minutes after initiating intravenous infusion of dopamine (10 μg/kg/min) following S-A node injury.

Middle panel : Five minutes after discontinuing dopamine infusion, heart rate slowed (165 beats/min) but ventricular beats persisted.

Right panel : Heart rate dropped to 140 beats/min and ventricular beats disappeared ten minutes after discontinuing dopamine infusion.

It is interesting that sinus rhythm reappeared despite injury of the S-A node.

D.C. = Discontinue

Fig. 6. Arrhythmia induced by dopamine and time-lag after discontinuing infusion

Some studies on the circulatory effects after open heart surgery have revealed that stroke volume is increased only slightly by inotropic agents[8)17)], and our results confirm that observation, especially with dopamine.

Although lidocaine may abbreviate sinus recovery time and allow entrance block to occur in patients with sinus node dysfunction[9)], no sinus arrest occurred in our experiments during lidocaine administration.

Conclusion

Dobutamine or dopamine was given to dogs with and without experimental S-A node injury. The degree of functional cardiovascular response produced by these two agents was compared, and the differences discussed. Dobutamine is superior to dopamine in causing little fluctuation of blood pressure and less tachycardia and arrhythmia. Since their effect on cardiac output is almost the same, we concluded that dobutamine might be an effective agent in patients with S-A node injury, sick sinus syndrome, high ventricular irritability state, as in ischemic heart disease, and low output state following cardiac surgery.

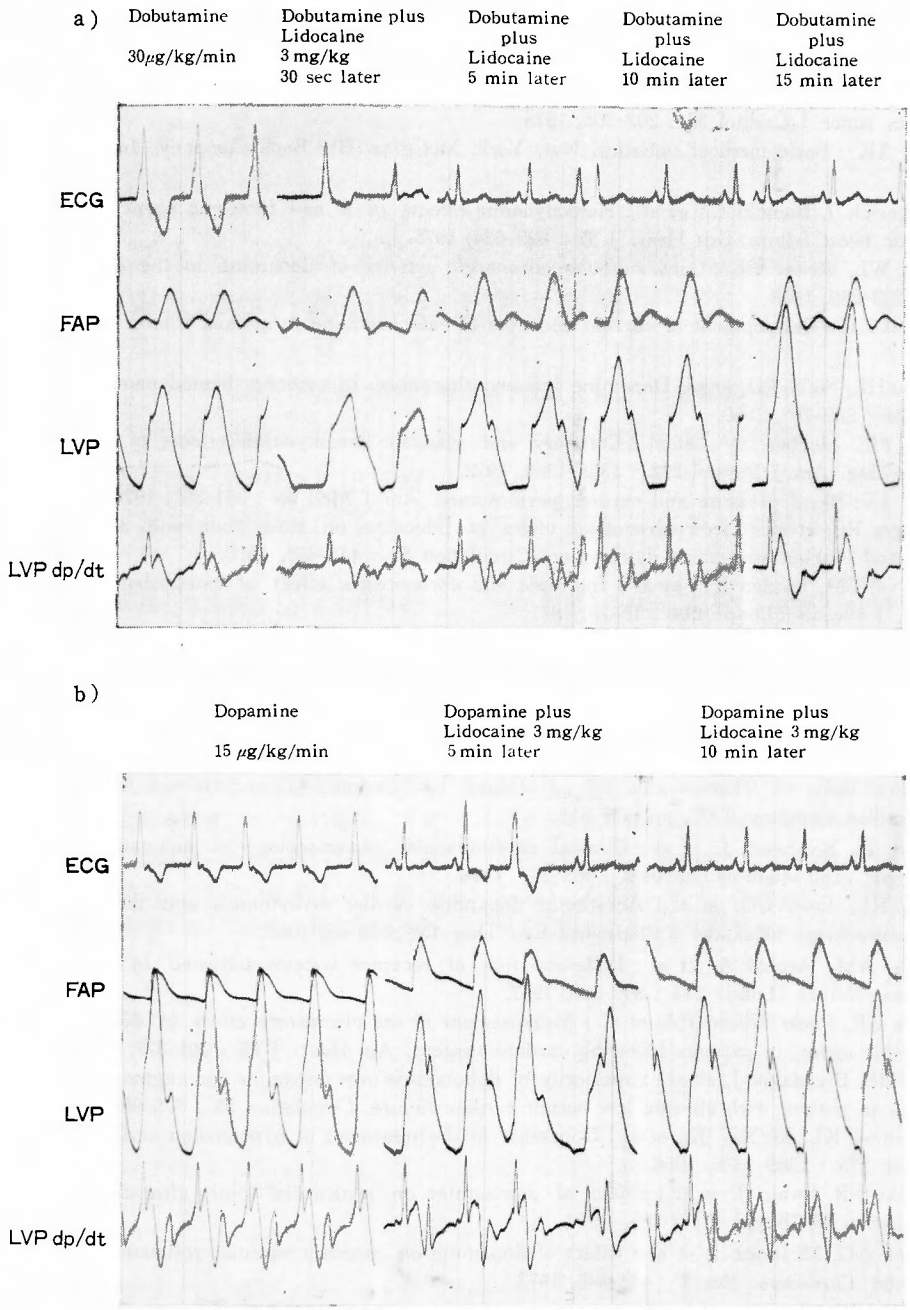


Fig. 7. Lidocaine was infused simultaneously with dobutamine or dopamine.
The LVP increased gradually after lidocaine (3 mg/kg) injection in dobutamine but not dopamine induced arrhythmia. However, the FAP gradually increased with both dobutamine and dopamine infusion. Arrhythmias disappeared ten minutes after lidocaine infusion.

a) Dobutamine-induced arrhythmia treated with lidocaine (after S-A node injury)

b) Dopamine-induced arrhythmia treated with lidocaine (after S-Anode injury)

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和文抄録

ドブタミンおよびドーパミンが実験的洞房結節障害犬の血行動態におよぼす影響

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上大静脈と右心房の移行部を中心とする部位の電気的焼灼によって洞房結節機能障害を作製し心原性循環障害を惹起せしめた実験犬を対象とし次の如き検討を行なった。

徐脈，心拍出量減少，血圧低下を来たした実験犬に対し，ドブタミンまたはドーパミンの静脈内点滴投与を行ない血行動態の変動を観察した．その結果，ドブタミン投与によって心拍出量は有意に増加したが，頻脈，不整脈の発生率は低く，血圧の変動も小さかった。一方ドーパミン投与によって心拍出量は同様に有意の増加をみたが，頻脈と心室性不整脈発生率はドブタミンの場合に比し有意に高く，同時に血圧の上昇が著明であった。これら両薬剤の投与によって発生した不整脈は薬剤の投与中止によって消失したが，リドカイン静脈内投与の併用は不整脈発生に対する抑制効果が認められた。以上の結果から，洞房結節障害あるいは洞不全症候群（sick sinus syndrome）を伴なう心低拍出症候群（low cardiac output syndrome）に対しては，ドブタミンはドーパミンよりも安全に使用し得る可能性のある薬剤であると思われる。